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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,990	07/09/2003	Henrik S. Olsen	PF108P2D1	8196

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EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,990	OLSEN ET AL.	
	Examiner	Art Unit	
	Christopher J. Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-28,30,31 and 139-155* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-28,30,31 and 139-155* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *16-28,30,31 and 139-155* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6.23.04 7.09.03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Response and Amendment filed 17 December 2004 has been received and entered in full.

Withdrawn Objections And/Or Rejections

2. The Objection to the Oath/Declaration as set forth at pp. 2 ¶2 in the previous Office Action (17 August 2004) is hereby *withdrawn* in view of Applicant's replacement Oath/Declaration (17 December 2004).

3. The Objection to the Specification as set forth at pp. 3 ¶3 in the previous Office Action (17 August 2004) is hereby *withdrawn* in view of Applicant's amendments (17 December 2004).

4. The Rejection of claim **16** under 35 U.S.C. §112 ¶1 as set forth at pp. 11- ¶21 in the previous Office Action (17 August 2004) is *withdrawn* in view of Applicant's submission of evidence of Deposit under the Budapest Treaty (17 December 2004).

New Objections

5. The amendment filed 17 December 2004 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: lines 5-7 of paragraph **[0114]** comprising the discussion of the antigenic epitopes and lines 7-10 of paragraph **[0115]** the discussion of the "at

least 7 contiguous amino acids in length" which add substantial new matter to the Specification as originally filed.

6. Applicant is required to cancel the new matter in the reply to this Office Action.

New Rejections as Necessitated by Amendment,

Rejections Maintained, and New Matter

(New Claims 140-155)

7. Claims **16, 24, 141,** and **150** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. The claims have been amended (or added) to include the limitation of "increase resistance of a mammalian cell to hypoxic stress" while is not support in the Specification for said limitation. In addition, the structure function combination of the structure of polypeptide of SEQ ID NO: 2 and the function of "increase resistance of a mammalian cell to hypoxic stress" does not have support in the Specification. The Specification does not teach which part of SEQ ID NO: 2 specifically has this activity.

Claim Rejections - 35 USC § 112

9. Claims **16-28, 30-31,** and **139-155** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a method of increasing resistance of a mammalian cell or a mammalian neural cell to hypoxic stress, comprising contacting the cell with a stanniocalcin polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and/or SEQ ID NO: 2 fused to a heterologous polypeptide*, does not reasonably provide enablement for *fragments, sequence variants, muteins of SEQ ID NO: 2, or non-mammalian cells.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims for the reasons as set forth at pp. 3-9 ¶4-14 in the previous Office Action (17 August 2004).

10. The Examiner notes that Applicant has added the new limitation of "capable of increasing resistance of a mammalian cell to hypoxic stress" to previously presented claims **16** and **24** and newly added claims **141** and **150**. Rejections to address this limitation are included herein.

11. Applicant traversed the rejection of the claims on the following grounds: **(a)** the enablement requirement requires nothing more than objective enablement unless there is reason to doubt the objective truth or accuracy of the statements, **(b)** screening for stanniocalcin fragments and/or variants does not preclude enablement of the invention, **(c)** the law does not require that Applicants forecast the results of an experiment before it is done, **(d)** the Specification provides ample guidance for one of ordinary skill in the art to make the stanniocalcin fragments and/or variants, **(e)** the skill in the art of molecular biology is high, **(f)** Verbost & Fenwick (May 1995) "N-terminal and C-terminal fragments of the hormone

stanniocalcin show differential effects in eels." Gen Comp Endocrinol. **98**(2): 185-92 supports the instant invention because of genetic conservation in mammals, and **(g)** only a reasonable correlation between *in vitro* and *in vivo* is required to meet the enablement requirement (Chandel *et al.* and Badr *et al*).

12. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

13. On "**(a)**", as discussed in the previous Office Action (17 August 2004) different stanniocalcin fragments have different effects (the examples of assays on mammalian bone). Since a compound and all of its properties are inseparable, it flows logically that different fragments of stanniocalcin (including the specific species of SEQ ID NO: 2), will have different effects on increasing resistance of a mammalian cell to hypoxic stress (including neural cells) (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). The instant Specification claims a large genus of stanniocalcin peptides (fragments, mutations, and variants of SEQ ID NO: 2) based on a single species (SEQ ID NO: 2) and thus fails to adequately support the claimed genus (see MPEP §2164.04).

14. On "**(b)**", while a routine amount of experimentation is permissible for inventions, the instant Specification does not disclose any guidance to undertake the screening to identify fragments and variants of the polypeptide of SEQ ID NO: 2 which are capable of increasing resistance of a mammalian cell to hypoxic stress. Therefore, provided Example 1, the skilled artisan is asked to undertake extensive, trial and error, experimentation to manufacture, isolate, and test innumerable mutations of the polypeptide of SEQ ID NO: 2 to identify the polypeptide muteins which satisfy the claims. The Specification has, in no way, provided conserved

structures, domains, motifs, active sites, or specific sequence tracts which are required to maintain the property claimed. As such, the instant claims represent an invitation to experiment as not guidance is presented to guide any experimentation.

15. On "**(c)**", no such requirement has been set forth. Title 35 U.S.C. §112 1st paragraph has two requirements, "make and use" and "material possession" (the first is discussed instantly and the second later in this Office Action). In the instant case, Applicant has only met these requirements for the stanniocalcin polypeptide of SEQ ID NO: 2. The law requires guidance in the form of motifs, conserved structures, domains, and/or specific sequence tracts which are necessary and sufficient for the stanniocalcin polypeptide of SEQ ID NO: 2 to retain the ability to increase resistance of a mammalian cell to hypoxic stress. As noted above, the Specification has suggested the skilled artisan undertake extensive and unguided experimentation as to find the mutations, deletions, and variants of the stanniocalcin polypeptide of SEQ ID NO: 2 which retain the ability to increase resistance of a mammalian cell to hypoxic stress. Thus the instant Specification has failed to meet the "make and use" requirement of Title 35 U.S.C. §112 1st paragraph for the full scope of the claims.

16. On "**(d)**", the instant Specification does not disclose any guidance to undertake the screening to identify fragments and variants of the polypeptide of SEQ ID NO: 2 which are capable of increasing resistance of a mammalian cell to hypoxic stress. No conserved structure, domains, motifs, or specific sequence tracts has been taught by the Specification to be required. As such, the instant claims represent an invitation to experiment as not guidance is presented to guide any experimentation.

17. On "**(e)**", regardless of the skill in the art, the instant Specification does not disclose the essential elements, functionally and structurally, for fragments and variants of the polypeptide of SEQ ID NO: 2 which are necessary and sufficient to increase resistance of a mammalian cell to hypoxic stress [see MPEP §2164.06(a)].

18. On "**(f)**", Verbost & Fenwick (May 1995) "N-terminal and C-terminal fragments of the hormone stanniocalcin show differential effects in eels." Gen Comp Endocrinol. **98**(2): 185-92 tested the effects of an N-terminal [peptide U ($eSTC_{1-20}$)], a C-terminal [peptide V ($eSTC_{103-136}$)], and a mid-fragment [peptide W ($eSTC_{202-231}$)] of stanniocalcin on plasma total and free (ionic) calcium levels and whole animal calcium influx in eels (Figure 1). Both the N- and the C-terminal fragments were hypocalcemic, causing 18 and 12% reduction in plasma calcium in stanniectomized eels, respectively. The N-terminal fragment caused more hypocalcemia than the C-terminal fragment. The mid-fragment had no effect on plasma calcium or calcium influx. Thus different STC fragments have different effects (Table 1). In addition, the STC fragments vary in their activity dependent upon the species in which it was tested due to differences in sequence among different STCs (pp. 190-191). This study does not support Applicant's instant claim of using fragments and variants of the polypeptide of SEQ ID NO: 2 increase resistance of a mammalian cell to hypoxic stress. The skilled artisan cannot gleam any support from Verbost & Fenwick (1995) to practice the instant invention, if they could, it would have been used as a prior art rejection. The Examiner notes that newly added claim 141 expands the scope of the claims to encompass non-mammalian cells. The Specification clearly demonstrates the activity of the polypeptide of SEQ ID NO: 2 on mammalian cells including mammalian neural cells, but not on non-mammalian cells. As discussed above, the stanniocalcin family is an ancient hormone family

and differs in its effects on animals. However, Applicant is correct in it is reasonable to expect mammalian cells to be similar in their response.

19. On "**(g)**", no such rejection was set forth in the previous Office Action (17 August 2004). The crux of the enablement rejection was the undue experimentation, lack of guidance, absence of species to support the genus, and the unpredictability of the art to establish that the instant Specification does not support the full breadth of the claims for all fragments and variants of the polypeptide of SEQ ID NO: 2 which are capable of increasing resistance of a mammalian cell to hypoxic stress.

20. Claims **16-28, 30-31,** and **139-155** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons as set forth at pp. 9-11 ¶15-20 in the previous Office Action (17 August 2004).

21. Applicant traversed the rejection of the claims on the following grounds: **(a)** the claims have been amended to include functional language ("capable of increasing resistance of a mammalian cell to hypoxic stress"), **(b)** the instant Specification contains description of numerous stanniocalcin fragments and variants (paragraphs **[0085]-[0109]**), and **(c)** the instant Specification provides an assay that may be carried out by one of ordinary skill in the art to test the fragments and variants of the polypeptide of SEQ ID NO: 2 for activity.

22. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

23. On "**(a)**", a sequence described only by a functional characteristic without any known or disclosed correlation between that function and the structure of the sequence is not sufficient to establish written description even when accompanied by a method of obtaining the claimed sequence (MPEP §2163).

24. On "**(b)**", while fragments and variants of the polypeptide of SEQ ID NO: 2 which are capable of increasing resistance of a mammalian cell to hypoxic stress may constitute a fecund ground for investigation, the CAFC ruled in *Genentech Inc. v. Novo Nordisk A/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner v. Manson,* **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CFAC stated that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to the any fragments and variants of the polypeptide of SEQ ID NO: 2 which are capable of increasing resistance of a mammalian cell to hypoxic stress. The full peptide alone, SEQ ID NO: 2, has the activity but no evidence that any fragments, sequences variants, or mutations thereof will. As such the instant claims represent an invitation to experiment.

25. On "**(c)**", to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the

genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a full-length protein and a property. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

26. See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al.* CAFC [(03-1304) 13 February 2004]. In *University of Rochester v. G.D. Searle & Co.* wherein the court rejected: "a patent directed to method for inhibiting prostaglandin synthesis in a human host using an unspecified compound, in order to relieve pain without the side effect of stomach irritation, did not satisfy the written description requirement of 35 U.S.C. §112. The patent described the compound's desired function of reducing the activity of the enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound. Since the invention consists of performing 'assays' to screen compounds in order to discover those with the desired effect, but the patent did not name even one compound that assays would identify as suitable for practice of the invention, or provide information such that one skilled in art could identify any suitable compounds. The specification did not indicate that compounds are available in public depository. The claimed treatment method cannot be practiced without the compound, and the inventors thus cannot be said to have 'possessed' the claimed invention without knowing of the compound or a method

certain to produce the compound." Thus said patent constituted an invitation to experiment to first identify, then characterize, and the use a therapeutic a class of compound defined only by their desired properties.

27. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Summary

28. No claims are allowed.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

30. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN
April 12, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
4-18-05